REMARKS

Reconsideration of this application is respectfully requested. Claims 21, 26, and 31 have been canceled, without prejudice or disclaimer. Claim 20 has been amended to clarify that the recited method is for treating a patient, and to recite a daily dose of 2.5 to 10 mg of escitalopram. Support for this amendment is found in the specification at, for example, page 5, line 29 to page 6, line 1. No new matter has been added. Claims 20, 22-25, 27-30, and 32-34 are pending and at issue.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 20-34 have been rejected under 35 U.S.C. § 112, second paragraph, as indefinite due to the term "less." While Applicants respectfully disagree with the Examiner, claim 20 has been amended to remove the term "less" and to specify a daily dose of 2.5 to 10.0 mg of escitalopram in order to expedite prosecution of this application.

Claim 21 has also been rejected as indefinite. Claim 21 as well as claims 26 and 31, which depended from claim 21, have been canceled in order to expedite prosecution. Therefore, this rejection is moot.

Accordingly, applicants respectfully request that these rejections be withdrawn.

Statutory Double Patenting Rejection

Claims 20, 22-25, 27-30, and 32-34 have been provisionally rejected under 35 U.S.C. §101 as claiming the same invention as claims 22, 24-29, 31-33, 36, and 38-40 of U.S. Patent Application No. 10/644,579 ("the '579 application").

Claims 20, 22-25, 27-30, and 32-34 in the present application are not identical to claims 22, 24-29, 31-33, 36, and 38-40 in the '579 application. For instance, claim 20 in the '579 application is

directed to a method of treating depression in a patient who failed to respond to initial treatment with a selective serotonin reuptake inhibitor ("SSRI") other than escitalopram. This patient population is different from the population called for in claim 20 of the present application (i.e., patients suffering from depression who have a sleep disturbance when treated with an SSRI other than escitalopram). A patient suffering from depression who has a sleep disturbance when treated with an SSRI other than escitalopram and has responded to treatment with the other SSRI would fall within the scope of the claims in the present application, but would not literally fall within the scope of the claims in the '579 application. Thus, claims 20, 22-25, 27-30, and 32-34 of the present application do not claim the same subject matter as claims 22, 24-29, 31-33, 36, and 38-40 of the '579 application. Accordingly, applicants respectfully request that this provisional rejection be withdrawn.

Obviousness-Type Double Patenting Rejections

Claims 20-34 have been provisionally rejected for obviousness-type double patenting over claims 21, 23, 25, 27, 29, 31, 33, 35, and 37 of U.S. Patent Application No. 10/644,588 ("the '588 application"), and claims 36-46 of U.S. Patent Application No. 10/468,685 ("the '685 application").

Submitted herewith is a terminal disclaimer over the '588 and '685 applications. Accordingly, applicants respectfully request that this provisional rejection be withdrawn.

Anticipation Rejections

Claims 20, 22, 24, 25, 27, 29-32, and 34 have been rejected under 35 U.S.C. § 102(b) as anticipated by Boegesoe (U.S. Patent No. Re. 34,712) or its European counterpart (European Patent No. 347066).

The rejection is respectfully traversed, and reconsideration is requested.

Claims 20, 22, 24, 25, 27, 29, 30, 32, and 34 are not anticipated by Boegesoe or its European counterpart because neither reference discloses treatment of the claimed patient population. The present claims are directed to a method of treating a patient suffering from depression who has a sleep disturbances when treated with an SSRI other than escitalopram. Boegesoe does not refer to patients who have sleep disturbances when treated with an SSRI other than escitalopram. Furthermore, not all depressed patients have sleep disturbances when treated with an SSRI other than escitalopram (i.e., sleep disturbances do not occur in all depressed patients treated with an SSRI other than escitalopram). In view of the foregoing, claims 20, 22, 24, 25, 27, 29, 30, 32, and 34 are not anticipated because each of the cited references fails to disclose each and every limitation of these claims. Accordingly, applicants respectfully request that this rejection be withdrawn.

Obviousness Rejections

Claims 21, 23, 26, 28, and 33 have been rejected under 35 U.S.C. § 103(a) as obvious over Boegesoe (or European Patent No. 347066) in view of Bouchard (*J. Affective Disorders*, 46:51-58 (1997)). The Examiner cites Boegesoe as disclosing administration of escitalopram to treat depression. The Examiner cites Bouchard as disclosing that "[s]ingle MADRS items analyses revealed a better effect of citalopram on 'reduced appetite' on day 14 and 42, and 'apparent sadness,' 'reduced sleep,' and 'suicidal thought' on day 42." *See* Office Action, p. 8. From this, the Examiner concludes that it would have been obvious to use escitalopram at a daily dose of 5-10 mg for the treatment of patients suffering from depression who have sleep disturbances.

Claims 21 and 26 have been canceled without prejudice.

To establish obviousness, there must be some teaching, suggestion, or motivation in the cited prior art that would have led a person of ordinary skill to combine or modify the references. *See In re*

Fine, 837 F.2d 1071 (Fed. Cir. 1988). Prior to the present invention, it was known that depressed patients treated with selective serotonin reuptake inhibitors (SSRIs) often exhibited sleep disturbances. *See* abstract for Asnis, et al., *J Clin. Psychiatry*, 60(10):668-76 (October 1999) (a copy of which is attached). It was, however, not known that the SSRI escitalopram does not induce sleep disturbances. Accordingly, one of ordinary skill in the art would not have been motivated to treat depression in a patient by administering escitalopram without inducing sleep disturbances, where the patient, when treated with an SSRI other than escitalopram, has sleep disturbances.

Furthermore, a finding of obviousness requires that there be a reasonable expectation of success when combining or modifying the cited references. *See* MPEP § 2142; *Brown & Williamson Tobacco Corp. v. Phillip Morris Inc.*, 229 F.3d 1120, 1124-25 (Fed. Cir. 2000); *Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320 (Fed. Cir. 2000) (stating that prior art references can only render a claim obvious where the combination of their teachings provides a reasonable expectation of success). Here, the cited references would not have provided one of ordinary skill in the art with a reasonable expectation of success in using escitalopram to treat depression *without inducing sleep disturbance* in a patient who has a sleep disturbance when treated with an SSRI other than escitalopram, as called for in the present claims. Rather, one of ordinary skill would have been discouraged from using escitalopram to treat these patients as it was known that depressed patients treated with SSRIs often exhibit sleep disturbances (*see* Asnis, et al., *supra*). Thus, without the knowledge that escitalopram does not induce sleep disturbances, one of ordinary skill in the art would not have had a reasonable expectation of success for using escitalopram to treat depression without inducing a sleep disturbance in such a patient.

In view of the foregoing, claims 23, 28, and 33 are not obvious over the cited references, and applicants respectfully request that this rejection be withdrawn.

Claims 20-34 have been rejected under 35 U.S.C. § 103(a) as obvious over Feighner (*J. Clin. Psychiatry*, 60(12):824-820 (1999)) in view of Hyttel (*J. Neural Transm.*, 88:157-160 (1992)) and Schoffers (*Tetrahedron*, 52(11):3769-3826 (1996)). (At page 10, line 1, the Office Action refers to Bouchard instead of Schoffers. This appears to be a typographical error in view of the discussion of Schoffers in the first full paragraph on page 11 of the Office Action.)

The Examiner cites Feighner as disclosing the use of citalopram at a dose of 10-60 mg, and estimates that this dose equates to 5-30 mg escitalopram. The Examiner acknowledges that Feighner does not teach the use of escitalopram or its oxalate salt. Hyttel is cited by the Examiner as disclosing escitalopram and its crystalline oxalate salt, and showing that the pharmacological activity of racemic citalopram is attributed to escitalopram. Schoffers is cited by the Examiner as disclosing the advantages of using chirally-pure compounds as pharmaceuticals. According to the Examiner, it would have been obvious to use a daily dose of 5-10 mg of escitalopram or its oxalate salt for treating depression without inducing sleep disturbances in patients who have sleep disturbances when treated with an SSRI other than escitalopram. The Examiner further contends that one of ordinary skill would have been motivated to decrease the dose level in or order to reduce side effects, and would have been motivated to use escitalopram in view of the advantages of chirally-pure drugs (as taught by Schoffer) and the teaching that the pharmacological activity of citalopram resides in escitalopram (as taught by Hyttel).

As discussed above, it was not known prior to the present invention that, unlike other SSRIs, escitalopram does not induce sleep disturbances. Without this knowledge, there would have been no motivation to select escitalopram for the treatment of a patient suffering from depression who has a sleep disturbance when treated with an SSRI other than escitalopram, as called for in the present claims. Likewise, without knowing that escitalopram is different from other SSRIs (i.e., because escitalopram

does not induce sleep disturbances), there would have been no reasonable expectation of success for using escitalopram to treat depression without inducing a sleep disturbance in such a patient.

For at least the foregoing reasons, claims 20, 22-25, 27-30, and 32-34 are not obvious over Feighner in view of Hyttel and Schoffers, and applicants respectfully request that this rejection be withdrawn.

Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining that the Examiner believes can be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: November 15, 2006

Respectfully submitted,

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J Clin Psychiatry. 1999 Oct;60(10):668-76.

Zolpidem for persistent insomnia in SSRI-treated depressed patients.

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BACKGROUND: Depressed individuals effectively treated with selective serotonin reuptake inhibitors (SSRIs) often report persistent insomnia and require adjunctive sleep-promoting therapy. METHOD: Men (N = 40) and women (N = 150) with a mean age of 41.6 years who had persistent insomnia in the presence of effective and stable treatment (at least 2 weeks) with fluoxetine (< or =40 mg/day), sertraline (< or =100 mg/day), or paroxetine (< or =40 mg/day) for DSM-IV major depressive disorder, dysthymic disorder, or minor depressive disorder of mild-to-moderate severity (and score of < or =2 on item 3 of the Hamilton Rating Scale for Depression [HAM-D]) participated in this randomized, double-blind, parallel-group study. At study entry, patients were required to score < or =12 on the HAM-D. During a 1-week single-blind placebo period, patients had to report on at least 3 nights a latency of > or =30 minutes or a sleep time of <6.5 hours and clinically significant daytime impairment. Patients received either placebo (N = 96) or zolpidem, 10 mg (N = 94) nightly, for 4 weeks and single-blind placebo for 1 week thereafter. Sleep was measured with daily questionnaires and during weekly physician visits. RESULTS: Compared with placebo, zolpidem was associated with improved sleep: longer sleep times (weeks 1 through 4, $p<.05$), greater sleep quality (weeks 1 through 4, $p<.01$), and reduced number of awakenings (weeks 1, 2, and 4; $p<.05$), together with feeling significantly more refreshed, less sleepy, and more able to concentrate. After placebo substitution, the zolpidem group showed significant worsening relative to pretreatment sleep on the first posttreatment night in total sleep time and sleep quality, reverted to pretreatment insomnia levels on the other hypnotic efficacy measures, or maintained improvement (fewer number of awakenings). There was no evidence of dependence or withdrawal from zolpidem (DSM-IV criteria). Incidence rates of adverse events were similar in both treatment groups (74% and 83% for placebo and zolpidem, respectively), but 7 zolpidem patients discontinued compared with 2 placebo patients. CONCLUSION: In this defined patient population, zolpidem, 10 mg, was effectively and safely co-administered with an SSRI, resulting in improved self-rated sleep, daytime functioning, and well-being.

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